

WELLCOME INSTITUTE LIBRARY	
Coll.	weTROmec
Call	pan
No.	WC 530
	188P7
	F 51m ^{3E}

THE MOSQUITO HYPOTHETICALLY CONSIDERED AS THE
AGENT OF TRANSMISSION OF YELLOW FEVER (1881.)

C.J.FINLAY

MEDICAL CLASSICS, 1937

THE WILLIAMS & WILKINS COMPANY

BALTIMORE, MARYLAND

1937-38



22200126606

MEDICAL CLASSICS

VOLUME II

563730

vol. 2., no. 6 (1938)



THE WILLIAMS & WILKINS COMPANY

BALTIMORE, MARYLAND

1937-38

INTRODUCTION

Yellow fever is a disease of tropical and sub-tropical countries, characterized by fever with jaundice, toxemia and albuminuria, and a tendency to hemorrhage, especially from the stomach.

This disease has been prevalent since the days of early history in the West Indies, in countries bordering on the Caribbean Sea, and on the west coast of Africa. Occasionally it has extended to the southern region of the United States, especially along the Atlantic seaboard. Serious epidemics of yellow fever have occurred as far north as Boston. Perhaps the most famous and serious attack of this disease in the United States took place in Philadelphia in 1793. In that city of 40,000 people, over 4,000 died in the period from August through November. Severe epidemics occurred in the United States occasionally throughout the 19th century and as late as 1903 a severe epidemic occurred in Texas near the Mexican Border.

Yellow fever has always been prevalent in Cuba. On that Island there was born in 1833 Carlos J. Finlay to whom goes the credit for first insisting that yellow fever was spread by mosquitoes. After being educated on the continent and in the United States, Finlay returned to his home in 1864, at the age of 31, and started a medical practice. Finlay's interest in yellow fever undoubtedly began at the time when he first realized that there was such a disease. We find him during his first year of medical practice gathering data on the climate of Havana. He was searching for a possible explanation of the mysterious outbreaks of yellow fever which occurred most seriously among white visitors to the Island. The natives had some immunity but nearly every foreigner contracted the disease within a year or two after arrival. Finlay noticed that when a boat anchored in the harbor of Havana and only the captain and mate came ashore, the crew being left aboard because of fear of contracting disease, nevertheless yellow fever broke out among the crew some time after the return of the captain and mate, even though these people continued in perfect health. Boats loaded at Havana sailed away to not-too-distant ports with their holds sealed. On arrival at a suitable and favorable port an epidemic of yellow fever broke out after the hold was opened. Finlay noticed also that yellow fever decreased when the temperature dropped to 50 or 60 degrees and the disease entirely disappeared when the freezing point was reached.

Dr. Finlay attempted to find one cause of the transmission of yellow fever which would explain all these startling facts. He probably thought first of personal and inanimate objects which had been in contact with patients (fomites). But transmission by these objects could not explain all the phenomena. Next Finlay considered flies as the go-between but this idea also had to

be discarded. Then this tireless worker decided that the mosquito was the agent of transmission of yellow fever.

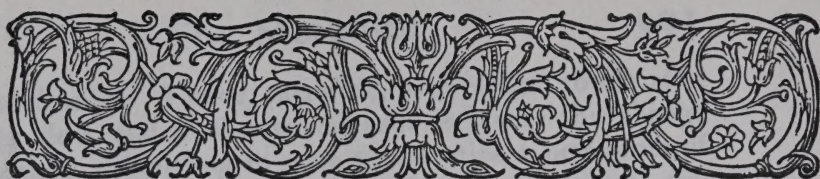
The following pages of Finlay's writings show the problem which he had set himself. In the first place, he had to find out all he could about mosquitoes existing in Cuba. Then he had to allow certain mosquitoes to bite patients ill with yellow fever and later these same mosquitoes to bite volunteer patients. Finlay very early decided, and correctly so, that the species of mosquito responsible for the transmission was the *Culex Cubensis*, later called the *Stegomyia Fasciatus*, and still more recently *Aedes Egypti*. But read in his own words, published in 1881, the story of Finlay's inspiration and the experiments he performed to prove the truth of his idea.

Unfortunately, Finlay never produced an undoubted case of yellow fever in his experimental subjects. It has since been found that an infected mosquito requires about twelve days after biting a patient ill with yellow fever before it can give the disease to a second victim. This fact escaped Finlay but does not detract from the greatness of his imagination.

When the Yellow Fever Commission of the United States Army was sent to Cuba in the last years of the 19th century their leader, Major Walter Reed, conferred with Carlos J. Finlay on the mosquito theory of transmission. At that time the *Bacillus icteroides* of Sanarelli (*Bacillus X* of Sternberg) was considered the causative agent. Reed and his Commission soon showed that this bacillus was not the culprit and proceeded to test Finlay's mosquito theory. The story of Reed and his Commission (James Carrol, Aristide Agramonte and Jesse W. Lazear who lost his life) is a famous story which must be deferred until a further time. The Commission proved that yellow fever is conveyed by the mosquito and within a year Major William C. Gorgas was eradicating yellow fever from Cuba by isolating patients ill with this disease and eliminating the mosquitoes. In three months Havana was free from the disease for the first time in 150 years. Gorgas later applied the same methods of control of yellow fever and other infectious diseases in the Panama Canal Zone and made it possible for the Canal to be constructed.

More recent work on yellow fever has been carried on by Hideyo Noguchi who, between 1918 and 1924, isolated and cultivated the causative organism *Leptospira interrogans* and developed a preventive vaccine and curative serum for the disease.

But to Carlos J. Finlay goes the credit for pointing out the way along which these other workers have progressed.



The Mosquito Hypothetically Considered as the Agent of Transmission of Yellow Fever

Read before the Royal Academy of Medical, Physical and Natural Sciences¹

Session of August 14th, 1881.

Published in *Trabajos Selectos del Dr. Carlos J. Finlay*, Secretaria de Sanidad y Beneficencia, Republica de Cuba, Habana, 1912, pp. 27-43

Mr. President, Gentlemen:

SOME years ago I had the honor to submit to your consideration the results of my alkalimetric experiments, by which I think I have definitely demonstrated the excessive alkalinity which prevails in the atmosphere of Havana. Some of the Members now present, may perhaps remember the relations which I then attempted to establish between that peculiarity and the development of yellow fever in Cuba. Much however has been done since that time, more accurate data have been obtained, and the etiology of yellow fever has been more methodically studied. In consequence thereof I feel convinced that any theory which attributes the origin and propagation of yellow fever to atmospheric influences, to miasmatic or meteorological conditions, to filth or to the neglect of general hygienic precautions, must be considered as

¹ Translated by Dr. Finlay from the *Anales de la Academia de Ciencias Médicas, Físicas y Naturales de la Habana*, Vol. XVIII, p. 147. Vide also *Revista de la Asociación Médico-Farmacéutica de la Isla de Cuba*, January 1902, p. 273.

utterly indefensible. I have, therefore, been obliged to abandon my former ideas, and shall now endeavor to justify this change in my opinions, submitting to your appreciation a new series of experiments which I have undertaken for the purpose of discovering the manner in which yellow fever is propagated.

In this paper I shall not concern myself with the nature or form of the morbid cause of yellow fever, beyond postulating the existence of a material, transportable substance, which may be an amorphous virus, a vegetable or animal germ, a bacterium, etc., but, at any rate, constitutes something tangible which requires to be conveyed from the sick to the (p. 28) healthy before the disease can be propagated. What I propose to consider is the means by which the morbid cause of yellow fever is enabled to part from the body of the patient and to be implanted into that of a healthy person. The need of an external intervention, apart from the disease itself, in order that the latter may be transmitted is made apparent by numerous considerations; some of them already pointed out by Humboldt and Benjamin Rush since the beginning of this century, and now corroborated by recent observations. Yellow fever, at times, will travel across the Ocean to be propagated in distant ports presenting climatic and topographic conditions very different from those of the focus from which the infection has proceeded, while, at other times, the disease seems unable to transmit itself outside of a very limited zone, although the meteorology and topography beyond that zone do not appear to differ very materially. Once the need of an agent of transmission is admitted as the only means of accounting for such anomalies, it is evident that all the conditions which have hitherto been recognized essential for the propagation of the disease must be understood to act through their influence upon the said agent. It seemed unlikely, therefore, that this agent should be found among Micro or Zoophytes, for those lowest orders of animal life are but little affected by such meteorologic variations as are known to influence the development of yellow fever. To satisfy that requisite it was necessary to search for it amongst insects. On the other hand, the fact of yellow fever being characterized both clinically and (according

to recent findings) histologically, by lesions of the blood vessels and by alterations of the physical and chemical conditions of the blood, suggested that the insect which should convey the infectious particles from the patient to the healthy should be looked for among those which drive their sting into blood-vessels in order to suck human blood. Finally, by reasons of other considerations which need not be stated here, I came to think that the mosquito might be the transmitter of yellow fever.

Such was the hypothesis which led me to undertake the experimental investigation which I shall here relate.

The application of the auxiliary sciences to Medicine often demands such a minute acquaintance with the different branches of human knowledge, that one cannot wonder at the length of time which sometimes elapses before certain facts recorded in a special branch can become available for purely medical investigations. This is particularly the case with regard to Natural History; its acquisitions being the outcome of the direct observation of Nature must, as a rule, undergo a complete revision from our own point of view before they can be turned to account in a nosological investigation. It has thus happened that more than a century after Réaumur had written his admirable Memoir on the habits of mosquitoes, justly considered as a model of accurate and keen observation, and which, (p. 29) from a general point of view, appears to exhaust the subject, when, six months ago, I recurred to that valuable source in search of data for the study which I had undertaken, I could not obtain the ones which I most needed. I was consequently obliged not only to go over all the data given by Réaumur, in order to ascertain whether they were also applicable to the Cuban mosquitoes, but to investigate other details about which neither Réaumur nor any other Naturalist had reason to be particularly interested.¹

¹ The truth of these remarks was well exemplified in the case of the mosquito which I had begun to investigate in December 1880, as may be seen from the following notes copied from a slip of paper upon which I had jotted down all the information that I obtained from the accomplished and well-known Cuban Naturalist D. Felipe Poey.

Havana, January 10, 1881, *Culex* mosquito, Robineau Desvoidy, Cuban mosquito. D. Felipe Poey took with him from Cuba to Paris some Cuban mosquitoes in 1817 or 1820, and they were there classified by Robineau Desvoidy.

D. Felipe Poey says that, in the same manner as happens with other insects, the male

Let us first recall the geographical distribution of mosquitoes. They may be said, in general terms, to exist everywhere, except at great altitudes above the sea-level. Many believe that the dipterous insect with which we are concerned, the genus "Culex", constitutes a special torment of the tropical regions, while in reality it is found in all latitudes. In the polar regions, the Laplanders, just as the inhabitants of the equinoctial regions of America, are prevented from taking their meals and from lying down to sleep within their huts, unless they surround themselves with an atmosphere of smoke in order to escape those pests. In the open, those insects will fly into their mouths and nostrils, and, notwithstanding the hardening of their skin during the previous winters, they find it necessary to use veils steeped in fetid grease and to anoint their bodies with cream or lard as a protection against mosquitoes. In Canada, in Russia, in England, in France, in Spain, all over Europe, in Siberia, China, the United States, in North and South America, mosquitoes abound. In Central Africa, a German explorer, Dr. Schwinfurst, was tormented by a "spotty-legged" species whose description might agree with that of the Cuban *C. mosquito*; and perhaps also the species observed in Batavia by Arnold, as stated by Dr. Kirby, who considers it as a non-descript variety, not unlike the *C. annulatus*, but without any spots on its wings.

(p. 30) In the same geographical position, however, the mosquito shows a disposition to spread over continents rather than to invade the islands, in accordance with Humboldt's observation that those insects are more abundant along the shores of large

dies after copulation, and the female after laying its eggs. That, in other respects, generation is accomplished under the same conditions as have been described regarding other species.

That the eggs of the Cuban mosquito, deposited upon the water, are black.

That in his opinion, if some mosquitoes do live as long as eight days, it must be because some accident has prevented the union of the male with the female.

The *Culex annulatus* has white rings upon its legs but its body is black; the *C. mosquito*, on the contrary (?), has silvery white plaques upon the last 5 articulations of its 3d pair of legs, 2 ill-defined ones upon the second pair, and two also on the other pair. The abdomen is white underneath. The thorax, he is informed, presents a central longitudinal line.

rivers than upon the islets and that mosquitoes are more troublesome close to the banks than in the centre of rivers. To this circumstance may, perhaps, be due the silence of the first chroniclers of the Discovery of America about mosquitoes, with reference to the first voyages of Columbus.¹ I have not found any mention of them with reference to the Antilles before 1538, when Hernando de Soto's soldiers having to cross a river near Puerto de los Principes, were so severely bitten by mosquitoes that large marks of blood appeared on their backs. To the comparative immunity of islands must probably be attributed the following account given to Osten Sacken (quoted in Brehm, V. IX, p. 446) by an American traveler. In 1823 mosquitoes were unknown on the Hawaiian Isles; but between 1828 and 1830 an old ship from Mexico was abandoned close to the shores of one of those islands. The inhabitants soon noticed around that spot some blood-sucking insects previously unknown to them; and the natives used to come in the evening to allow themselves to be bitten by those extraordinary insects. Mosquitoes afterwards multiplied and spread on those islands, developing into a regular plague.

Although mosquitoes are found in all latitudes, their abundance varies in different localities. Humboldt and Bonpland, in their *Travels in Equinoctial America* wrote: "The annoyance suffered from mosquitoes and "zancudos" in the torrid zone is not so general as most people think. On the high plateaux more than 4000 toises (2500 feet) above the sea-level, and in very dry plains, far from large rivers, such as Cumana and Calabozo, gnats are not much more abundant than in the most populous parts of Europe." The influence of dryness and of a long distance from water-courses, pointed out by those travelers, is easily understood, inasmuch as the larvae and pupae of the mosquitoes are aquatic, and the winged insect requires water for the laying and hatching of its eggs. The impediment to their propagation at high levels may consist in the exaggeration of the difficulty which those insects must always experience in flying

¹ This is a mistake, for I have since found the abundance of mosquitoes on the Island Hispaniola specially mentioned in Herrera (*Década I, Lib. V, cap. XI, p. 179*).

upwards after they have filled themselves with blood; a difficulty which will be much more marked in a species having such small wings as those of the *C. mosquito*. The rarefaction of the atmosphere at those great heights necessarily increases that difficulty, and, under those circumstances, the mosquito will instinctively shun those localities. The above mentioned travelers also relate that a missionary priest, Bernardo Zea, had built himself a room over a scaffolding of palm boards, and they (p. 31) used to go there at night to dry their plants and to write their Diary, adding: "The missionary had rightly observed that those insects are more numerous in the lower strata of the atmosphere, within 12 to 15 feet from the ground." Further on they write: "As one proceeds towards the plateau of the Andes, those insects disappear and the air one breathes becomes pure. . . . at a height of 200 toises (1500 feet) mosquitoes and zancudos are no longer feared".

Historically the mosquito is one of the insects most anciently observed. Aristotle and Pliny refer to its proboscis which serves both for piercing the skin and for sucking the blood. The Greek historian Pausanias, according to Taschenberg, mentions the city of Myus, in Asia Minor, situated on a bay which had formerly communicated with the sea but was afterwards cut off from it; when the water in the lake which was thus formed ceased to be salt, such a plague of mosquitoes was developed that the inhabitants had to abandon the city and betook themselves to Miletus. So also in the *Decades of Hereera*, we read that Juan Grijalva when he first discovered the coast of New Spain (Mexico), in 1518, landed with his men on an islet which he named San Juan de Ulua, and they had to build their huts "at the top of the highest sand-mounds which they could find in order to avoid the importunity of mosquitoes." Seven days later, Bernal Diez del Castillo had to seek protection in some Indian places of worship, "unable to stand the mosquitoes." Finally, in 1519, on the same spot where Veracruz now stands, according to Herrera "the long-legged mosquitoes and the small ones which are still worse used to worry the people who went with Cortes."

I have observed two kinds of mosquitoes in Havana since

December last, when I began to study those insects. One species is large, of a yellowish colour, with thin, long legs, and without any particular markings; I suppose it must be the identical *zancudo* which worried Cortes' men on the sandy plains of San Juan de Ulua in 1519, and the same which La Sagra describes as the *Culex Cubensis*. The length of its body, measured from the root of the proboscis to the anal extremity, varies between 5 and 7 millimetres. This species comes out exclusively at night, generally between 9 and 10 o'clock, and pursues its annoying evolutions until daybreak. All the specimens which I have found inside of mosquito-nets (in the morning) have belonged to that species; and they remain part of the day in that position digesting the blood which they have sucked. The other species is the *Culex mosquito*, specimens of which were taken to Paris by the distinguished Cuban Naturalist, Felipe Poey, in 1817 or 1820, and were there classified by M. Robineau Desvoidy under that name. I have noticed two varieties of this species: one large, with a slight, graceful figure, vigorous, of a dark gray color, somewhat smaller than the *C. Cubensis*; the other only measures from 4 to $4\frac{1}{2}$ millimetres. I have (p. 32) not sought for particular differential characters between these two varieties of the same species, their respective size sufficing for my present object. Both varieties of the *C. mosquito* present the following distinctive characters: the body is dark colored, sometimes almost black or steel-colored; the ventral segments of the abdomen as well as the dorsal ones appear strengthened by an outer layer, with white rings corresponding to the inter-spaces, though sometimes (on the ventral side) the segments are whitish and the inter-spaces are dark. On each side of the abdomen there are two rows of pearly-white dots, between which, after feeding, a transparent membrane stretches allowing the blood or other contents of the distended stomach and intestine to be seen. Upon the hind legs there are five very characteristic white rings, corresponding to the articulations of the tarsus, metatarsus and tibia; the latter sometimes presenting a sixth white spot. The middle and front legs present two or three white rings. Upon the sides of the thorax are seen 8 or 10 white dots or patches of irregular

outline, and upon the antero-superior surface of the thorax a combination of white lines on a dark background is seen resembling a two-stringed lyre. The palps and the antennae also carry some white marks. Some of the aforesaid markings are apt to be effaced with age or by friction, but the most characteristic ones very seldom disappear. The wings of the *C. mosquito*, the venation of which I shall not describe at present, have no spots like those of the European *Culex annulatus*; and its wings are so short that, when closed, they leave the last segment of the body uncovered. Of course, in order to observe the characters which I have been describing it is necessary to use a magnifying glass; aplanatic lenses of $2\frac{1}{2}$ or 3 inches focus are very convenient for that purpose.

The males of both species are readily recognized by their feathery antennae, like a pair of mustachios, and by its three-pronged proboscis due to the long palps which lie close to the proboscis above, but stand out on each side near the point; thereby showing a marked contrast with the smooth proboscis of the female whose short palps barely cover the upper sixth of its length.

The two species of mosquitoes to which I have referred do not come out at the same hours: the zancudo comes out at night and the *C. mosquito* in the daytime. This distribution of the day and night between the two species made me think that the zancudo, notwithstanding its larger size and more robust appearance, might not be constituted to stand the heat of our summer sunshine. I tried, therefore, the following experiment. On the 9th of June, at noon, I exposed to the direct rays of the sun the bulbs of my psychrometer; after half an hour the dry bulb marked 42° . 25 C. and the wet bulb 31° .75. I then substituted in place of the instrument a tube in which a zancudo had been confined for 5 days, but continued (p. 33) lively and agile; after 5 minutes' exposure the insect was dead. I then substituted another tube containing a *Culex* mosquito, and after leaving it exposed to the sun during 15 minutes it was still alive and continued to live another 24 hours in its tube.

It is well known that only the female mosquitoes bite and suck

blood, while the males feed on vegetable juices, principally the sweet ones; but I have not found it mentioned in any author that even the females never bite before having been fertilized. This, at least, I infer from the following experiments.

A female *C. mosquito*, caught soon after breaking loose from its pupa-case, and kept alive during three days, cannot be got to bite during that space of time. I have several times repeated the experiment and always with a negative result.

Female mosquitoes which are caught pairing bite and suck blood readily very soon after they are parted.

Finally, those which are caught in the act of biting and sucking blood, will as a rule, lay eggs after a few days, while the fertilized females which have not been allowed to suck blood die without every laying any ova.

We are thus led to infer that the craving of the female mosquito for live blood is not meant to supply an indispensable article of food. Indeed it seems improbable that for the nourishment of so small a body, such a disproportionate quantity of rich blood be needed. I have come to the conclusion that the sucking of blood is intended for another object connected with the propagation of the species. The likeliest hypothesis seems to be that the feed of blood acts through the degree of heat which it procures. If, for instance, the maturation of the ovules contained in the ovaries of the mosquito demands a temperature of 37°C. , the latter could scarcely be obtained by any other means so readily as by the insect filling itself with a fair amount of blood of that temperature; and sometimes it may be more convenient for the mosquito to bite a patient attacked with fever, whose blood at 39° or 40° may prove more efficacious in hastening the process of ovulation. It will thus be understood why large insects like the zancudo are able to absorb with a single bite the amount of blood required for the maturation of all the 200 to 350 ova which they lay at one sitting, while the smaller species, like the *C. mosquito*, have to bite and fill themselves several times with blood before beginning to lay, and generally require several sittings before all their ova are laid.

After the female mosquito has filled itself with blood it requires

two, three or four days, according to the species (*and the season of the year*) to complete the digestion of its feed; and, during that time, remains out of sight spending hours in a curious performance the object (p. 34) of which Réaumur did not understand, having only observed it in the open. When the insect is confined in a glass tube, it is easy to see that the performance consists in besmearing every part of its body with a secretion which is picked up from the anal extremity with its hind legs and smeared successively upon the legs, the abdomen, the wings, the thorax, the head and even the proboscis. As suggested by Felipe Poey, *facile princeps* among our Cuban Naturalists, the object of this operation is probably to make the mosquito water-proof before it goes to the water to lay its eggs. During the digestion, the mosquito also drops some bloody particles or excrement which present the peculiarity of being extremely soluble in water, even after being kept in a dry condition during several months. This is probably due to the admixture of the blood with the saliva poured out during the process of biting, and which is generally believed to render the blood more fluid while it is being sucked by the insect. As a rule after a complete, uninterrupted feed of blood, the mosquito does not bite again, and even shuns the contact of the bare skin (perhaps because the heat of it becomes at that time disagreeable) until the digestion of the blood has been completed. With the zancudo (night-mosquito) it is at that time that its ova are laid.

I shall not reproduce the classical description given by Réaumur of the manner in which the female of a European species, *Culex pipiens*, builds its tiny boat of eggs and floats it on the water. The *zancudo* of Cuba goes through a similar performance; but after having launched their little boat of eggs, they often stretch themselves out to die upon the water, and I have wondered whether the dead insects which Réaumur attributes to newborn ones which have been wrecked and drowned at the moment of leaving their pupa-shell might not be the cadavers of mothers who had died in order that their bodies should remain close to the ova so as to contribute to the feeding of their progeny.

The three successive operations: fertilization, sucking of blood

and laying of eggs, constitute the most essential phases of the mosquito's existence. The first of these operations, as in most other insects, probably, need not occur more than once in order that the impregnated seminal sack of the female shall retain the faculty of fertilizing all the ova which may thereafter traverse its oviducts. In the Cuban bee, according to Felipe Poey, a single fecundation by the male, suffices for all the thousands of eggs which the female bee lays during the two or three years of its life. With the females of the various species of the genus *Culex*, which, till now, had been observed, there had been no occasion to test whether such a prolonged fertilizing faculty existed, inasmuch as all their ova were laid at a single sitting; but the case is different with the females of the *Culex* mosquito. These lay their ova separately or in files of 9 to 15 either isolated or in groups, sometimes upon the water (p. 35) or else upon solid bodies not too far removed from the level of the water, so that a moderate elevation of that level will allow the water to cover them. My explanation about the need of several bites and feeds of blood before the *C. mosquito* is able to lay all its ova, maybe purely hypothetical; it is nevertheless a fact that the females of that species are always ready to bite a second time after they have digested all the blood which had been sucked at a previous bite. A female *C. mosquito*, caught (in Havana) in January of the present year, had bitten 12 times and laid eggs three times in the course of the 31 days which it lived; its death having occurred in New York where it was exposed to temperature below the freezing point.

With the captive females of the *C. Cubensis* (*C. Pungens*), I have never been able to obtain a second bite, whether it had or had not laid its ova. Possibly, however, when at large they may need to bite several times before laying; for I have occasionally seen them come to bite my hand, with some blood already in their stomach. This I have attributed to a previous bite which had been interrupted before the insect had been able to draw its full allowance of blood.

Evidently, from the point of view which I am considering, the *Culex* mosquito is admirably adapted to convey from one person

to another a disease which happens to be transmissible through the blood; since it has repeated opportunities of sucking blood from different sources, and also of infecting different persons; so that the probabilities that its bite may unite all the conditions required for the transmission will thereby be greatly increased. On the other hand, inasmuch as the *C. Cubensis* absorbs a larger quantity of the infectious blood at each feed, its mouth-parts may retain a larger amount of virus, and perhaps produce a graver inoculation when it happens to attack a non-immune a few moments after having bitten the patient, its first bite having been interrupted. In that case, a graver infection might result but the chances of its occurring would be much less.

In order to understand the special facilities which the bite of the *C. mosquito* affords for the inoculation of any infectious particles which should be contained in the blood, it is necessary to have some idea of the disposition and structure of the apparatus used by the female mosquito in its operation of stinging and of sucking blood.

What is seen of the proboscis, under ordinary circumstances is the sheath, which represents a modified nether lip. It arises from a pedicle attached to the base of the head, below the other mouthparts. It is slit along its upper border as far as the terminal, conical button seen at its free end, and which, I believe, is formed by two labial palps. From the extremity of this button the other pieces constituting the sting are protruded (in the act of stinging). The sheath of the *C. mosquito*, to (p. 36) which species my observations have been limited, measures $2\frac{1}{2}$ millimeters; that of the species observed by Réaumur measured according to that author, *one French line*; and as our mosquito oftentimes drives its sting nearly to its very root, it can readily reach a blood-vessel at a depth not exceeding $\frac{1}{5}$ of a centimetre. In the interior of the sheath are two tubes, lying apparently loose at the bottom of its concavity; I have observed them presenting a tortuous direction, and uniting into a common trunk within the concavity of the pedicle. I believe it is through these tubes that the mosquito pours out the acrid saliva which causes the burning sensation during its bite, and which, according to

naturalists, serves to render more fluid the blood which has to run through the sucking apparatus.

Within the sheath are contained five pieces: the principal one constitutes the labrum or upper-lip, it is of a horny consistence and prolonged like a long spur, deeply grooved so as to form a canal opening upwards¹ and ending in a point like that of a tooth-pick cut out of a long slender quill. This piece is rigid and presents on its outer surface a curious design as if covered with a net whose meshes, in relief, form small parallelograms with acute angles pointing longitudinally. Perhaps within those innumerable meshes might be lodged some particles of the blood sucked by the insect. The other four pieces are paired, flexible setae, two of them constituting the mandibles, and the others the maxillae. The structure of the two pairs is very different in each. The mandibles are concave inwardly, and have a tendency to maintain a curvilinear direction; their outer side is convex and presents transverse ridges ending on their free border in very minute teeth. The point of the mandibles is curved and armed to its very end with teeth which appear to be both sharp and strong. The maxillae are inserted a little below the mandibles; they present the appearance of a ribbon with its edges turned in like a seam, armed with a fringe of long delicate teeth; its general aspect is that of a long narrow blade of grass, ending in a broad double-edged point and strengthened by a longitudinal vein running all along its middle. All these setae adapt themselves upon the stem of the labrum so closely that, after the sheath has been removed and before the setae are dissociated, one would never think that the round or oval rod, with its sharp, single point, which comes into view is an assemblage of the five separate pieces which I have been describing.²

¹ This is a misprint. It should read "downwards."

² The above description was written under the impression that only 5 mouth parts went to constitute the sting of the *Culex* mosquito, and of mosquitoes in general. Soon after writing this paper, however, I became aware of the existence of a sixth seta, in accordance with the statements of modern entomologists.—On closer observation too, I found that what I had described as one of the mandibles, more properly applies to the hypopharynx, about the existence of which I was at that time ignorant. I append therefore a reproduction of a drawing which I made in 1882 or 83 of the six mouth parts of the

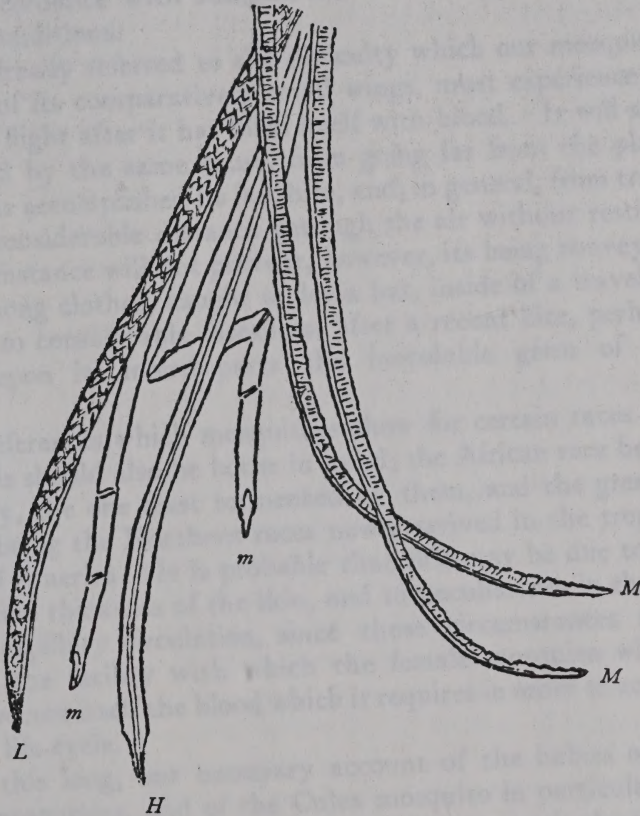
The mosquito commences its operation of stinging by tentatively exploring the skin with the point of its proboscis until it finds a suitable spot. It then takes a firm position upon its six feet (sometimes the two hind legs are raised above its back), the thorax is strongly bent down while the head and the proboscis assume a vertical position. Next, with the naked eye or, better, with the assistance of a magnifying glass, the sheath is seen to bend backwards, at its upper part, gradually assuming the shape of an horizontal < the two branches of which gradually come closer together as the sting penetrates deeper into the skin. The sting is then seen as a very slender wire stretching between the extremities of the horizontal < figured by the sheath, and moving up and down in unison with the maxillary palps, until a blood-capillary has been reached. The insect remains motionless while it fills itself, apparently without effort, with the red warm blood of its victim. During the bite a sharp, instantaneous, burning sensation is sometimes felt, owing to the saliva which the mosquito instils into the wound through the end of the sheath, the conical extremity of which remains caught between the edges of the wound. The insect's stomach becomes distended and the blood is seen through the transparent lateral walls of its body. Several minutes are generally required for the completion of the operation; as long as seven in some cases which I have timed.

It is a well-known fact that, while mosquitoes are never wholly absent (p. 38) from Havana, they are much more abundant at some seasons of the year. It appears to me that they increase in numbers from April or May till August, and thereafter gradually decrease till February or March. Another point, however,

sting.—Regarding the existence of one or two tortuous tubes with striated walls, occupying the concavity of the sheath, and which I considered as the excretory duct of the salivary glands, I have met with it on several occasions and still believe that in the species which I am considering the salivary duct may not empty itself into the tube of the hypopharynx, but runs through its base lying free in the concavity of the sheath. This supposition has been strengthened in my mind by a precedent which I have just read in Packard's Text-Book of Entomology, p. 78 where he quotes from Meinert the following:

"The efferent duct of the thoracic salivary glands (ductus salivalis) perforates the hypopharynx, more or less near the base, that the saliva may be ejected through the canal into the wound, or that it may be conducted along the labellae. *Very rarely the salivary duct perforating the hypopharynx, is continued in the shape of a free, very slender tube.*"

requires to be borne in mind, inasmuch as it affords an explanation of the recurrence, hitherto unaccounted for, of yellow-fever epidemics without new importation, in localities previously considered as immune. I allude to the hibernation of mosquitoes, a phenomenon which is not observed in our climate, at least in



L, labrum; *m*, maxillae; *H*, hypopharynx; *M*, mandibles

all its phases; but which constitutes, according to the best authorities, the regular mode by which the species is propagated in cold climates, during winter. Taschenberg informs us that: "the fertilized females of the last generation hibernate during winter in out-of-the-way places such as the cellars of dwellings, and set about propagating their species the following spring."

Among the conditions which favor the development of mosquitoes may be mentioned; heat, moisture, the vicinity of stagnant waters, low, dark localities sheltered from the wind, and the summer-season. It is necessary, however, to bear in mind Humboldt's observation that the abundance of mosquitoes is not always in accordance with recognizable meteorological or topographical conditions.

I have already referred to the difficulty which our mosquito, by reason of its comparatively small wings, must experience in its upward flight after it has filled itself with blood. It will also be hindered by the same cause, from going far from the place where it has accomplished its last bite, and, in general, from traveling any considerable distance through the air without resting. This circumstance will not prevent, however, its being conveyed, hidden among clothes, caught under a hat, inside of a traveling bag, etc., to considerable distances, after a recent bite, perhaps carrying upon its mouth-parts the inoculable germ of the disease.

The preferences which mosquitoes show for certain races and individuals should also be borne in mind; the African race being, apparently, the one least tormented by them, and the greatest sufferers being the Northern races newly arrived in the tropical regions of America. It is probable that this may be due to the comparative thickness of the skin, and to peculiarities in the cutaneous capillary circulation, since those circumstances must influence the facility with which the female mosquito will be able to procure itself the blood which it requires in order to accomplish its life-cycle.

After this long, but necessary account of the habits of our Cuban mosquitoes, and of the *Culex* mosquito in particular, let us consider by what means that insect might transmit the yellow fever, if that disease happens to be really transmissible through the inoculation of blood. The first and most natural idea would be that the transmission might be effected (p. 39) through the virulent blood which the mosquito has sucked, amounting to 5 and even to 7 or 9 cubic millimeters, and which, if the insect happens to die before completing its digestion, would be in ex-

cellent condition to retain during a long time its infecting properties. It might also be supposed that the same blood which the mosquito discharges, as excrement, after having bitten a yellow fever patient, might be dissolved in the drinking water, whereby the infection might be conveyed if the latter were susceptible of penetrating by the mouth. But the experiments of Ffirth and other considerations arising from my personal ideas regarding the pathogenesis of yellow fever, forbid my taking into account either of those modes of propagation, as I shall now explain. When the U. S. Yellow-fever Commission took their leave, two years ago, they presented us with a valuable collection of micro-photographs from preparations made by our corresponding Member, Dr. Sternberg, showing what, to me, appeared to be a most striking feature, namely, that the red blood-globules are discharged unbroken in the hemorrhages of yellow-fever. This fact taken in connection with the circumstance that those hemorrhages are often unattended with any perceptible break in the blood-vessels, while, on the other hand, they constitute a most essential clinical symptom of the disease, led me to infer that the principal lesion of yellow fever should be sought for in the vascular endothelium. The disease is transmissible, it attacks but once the same person, and always presents in its phenomena a regular order comparable with that observed in the eruptive fevers, all of which circumstances suggested to my mind the hypothesis that yellow-fever should be considered as a sort of eruptive fever in which the seat of the eruption is the vascular endothelium. The first period would correspond to the initial fever, the remission to the eruptive period, and the third period would be that of desquamation. If the latter phase is accomplished under favorable conditions, the patient will only show evidence of an exaggerated transudation of some of the liquid elements of the blood through the new endothelium; if the conditions are unfavorable, a defective endothelium will have been produced, incapable of checking the figured elements of the blood: passive hemorrhages will occur and the patient may find himself in imminent danger. Finally, assimilating the disease to small-pox and to vaccination, it oc-

curred to me that in order to inoculate yellow fever it would be necessary to pick out the inoculable material from within the blood vessels of a yellow-fever patient and to carry it likewise into the interior of a blood vessel of the person who was to be inoculated. All of which conditions the mosquito satisfies most admirably through its bite, in a manner which it would be almost impossible for us to imitate, with the comparatively coarse instruments which the most skillful makers could produce.

Three conditions will, therefore, be necessary in order that yellow (p. 40) fever may be propagated: 1. The existence of a yellow fever patient into whose capillaries the mosquito is able to drive its sting and to impregnate it with the virulent particles, at an appropriate stage of the disease. 2. That the life of the mosquito be spared after its bite upon the patient until it has a chance of biting the person in whom the disease is to be reproduced. 3. The coincidence that some of the persons whom the same mosquito happens to bite thereafter shall be susceptible of contracting the disease.

The first of these conditions, since Dr. Ambrosio G. del Valle has been publishing his valuable mortuary tables, we may be sure, has never failed to be satisfied in Havana. With regard to the 2d and 3d, it is evident that the probabilities of their being satisfied will depend on the abundance of mosquitoes and on the number of susceptible persons present in the locality. I firmly believe that the three above mentioned conditions have, indeed, always coincided in years when yellow fever has made its greatest ravages.

Such is, Gentlemen, my theory; and I consider that it has been singularly strengthened by the numerous historical, geographical, ethnological and meteorological coincidences which occur between the data which I have collected regarding the mosquito and those which are recorded about the yellow fever; while, at the same time, we are enabled by it to account for circumstances which have until now been considered inexplicable under the prevailing theories. Yellow fever was unknown to the white race before the discovery of America, and, according to Humboldt, it is a tradi-

tional opinion in Vera Cruz that the disease has been prevailing there ever since the first Spanish explorers landed on its shores. There also, as we have seen, the Spaniards since their first landing have recorded the presence of mosquitoes; and with greater insistance than in any other place in America, in the identical sand-mounds of San Juan de Ulloa (the present site of Veracruz). The races which are most susceptible to Yellow fever are also the ones who suffer most from the bites of mosquitoes. The meteorological conditions which are most favorable to the development of yellow fever are those which contribute to increase the number of mosquitoes; in proof of which I can cite several local epidemics regarding which competent authorities assert that the number of mosquitoes during the prevalence of yellow fever was much greater than on other occasions; indeed, it is stated in one instance that the mosquitoes were of a different kind from those which were usually observed in the locality, having gray rings around their bodies. Regarding the topography of the yellow fever, Humboldt points out the altitudes beyond which mosquitoes cease to appear, and in another passage gives the limits above the sea-level within which the yellow fever may be propagated. Finally, in the notorious case of the U. S. Steamship Plymouth, in which two cases of yellow fever occurred at sea, after the vessel had been disinfected and frozen during (p. 41) winter, four months after the last previous case had occurred on that vessel (the preceding November), the facts can be readily accounted for by the hibernation of mosquitoes which had bitten the former yellow fever patients, and, which, upon finding themselves again within tropical temperatures, recovered from their lethargic condition and bit two of the new men of the crew.

Supported by the above reasons, I decided to submit my theory to an experimental test, and, after obtaining the necessary authorization, I proceeded in the following manner.

On the 30th of last June, I took to the Quinta de Garcini a mosquito which had been caught before being allowed to sting, and there made it bite and fill itself with blood from the arm of a

patient, Camilo Anca, who was in the fifth day of a well characterized attack of yellow fever of which he died two days later. I then picked out F. B., one of twenty healthy non-immunes who have continued until now under my observation, and made the same mosquito bite him. Bearing in mind that the incubation of yellow fever, in cases which allow its limits to be reckoned, varies between one and fifteen days, I ordered the man to be kept under observation. On the 9th of July, F. B. began to feel out of sorts, and on the 14th he was admitted to the Military Hospital with a mild attack of yellow fever perfectly characterized by the usual yellowness, and albumin in the urine which persisted from the third till the ninth day.

On the 16th of July, I applied a mosquito at the same Quinta de Garcini, to a patient, Domingo Rodríguez, in the third or fourth day of yellow fever; on the 20th, I allowed the same mosquito to bite me and, finally, on the 22nd I made it bite A. L. C., another of the 20 men who are under observation. Five days later, this man was admitted at the Hospital with fever, severe headache, pain in the loins and injected eyes; these symptoms lasted three days, after which the patient became convalescent without having presented any yellowness nor albuminuria. His case was, however, diagnosed as "abortive yellow fever" by the physician in charge.

The 29th of July, I made a mosquito bite D. L. R. who was going through a severe attack of yellow fever at Quinta de Garcini, being then in its third day. On the 31st, I made the same mosquito bite D. L. F., another of my 20 men under observation. On the 5th of August, at 2 a. m., he was attacked with symptoms of mild yellow fever; he subsequently showed some yellowness but I do not think that he developed any albuminuria; his case was, nevertheless, diagnosed "abortive yellow fever."

Finally, on the 31st of July, I applied another mosquito to the same patient, D. L. R. at Quinta Garcini, his attack having then reached its fifth day and proving fatal on the following one. On the 2d of August I applied this mosquito to D. G. B., another of my twenty non-immunes. Till the (p. 42) present date (12th)

this last inoculation has not given any result; but, as only 12 days have elapsed, the case is still within the limits of incubation.¹

I have to state that the persons mentioned above are the only ones who were inoculated with mosquitoes, in the manner described; and that since June 12th, till now (in the course of seven weeks), barring my first three inoculated men, no other case of confirmed or abortive yellow fever has occurred among the twenty non-immunes, whom I have had under observation.²

These experiments are certainly favorable to my theory, but I do not wish to exaggerate their value in considering them final, although the accumulation of probabilities in my favor is now very remarkable. I understand but too well that nothing less

¹ This inoculated man D. G. B., came to my office on the 17th of August to be inspected, stating that during the previous six days he had been suffering from headache, loss of appetite and general malaise. On the 24th I found that he had fever (Pulse 100, Temp. 30.1), and he stated that it had been higher on the previous day and also that same morning. The fever however was never severe, and the patient did not report himself sick nor take any medicine. The fever ceased, but the pain in the head continued a few days longer.

Another of my 20 non-immunes was bitten on the 15th of August by a mosquito which, 2 days before, had bitten a patient in the Military Hospital, in the 5th day of yellow fever. This inoculated man does not appear to have been sick so far (September 1st). I have not been able to see him since his inoculation, and it is only from hearsay that I have been informed that he has felt poorly on the 24th and 25th of August; but did not report himself sick.

² There was a fourth case which was also diagnosed as "abortive yellow fever" at the Military Hospital, but regarding whose diagnosis Dr. Delgado and I were doubtful. He was one of the 20 non-immunes of our group, and a different kind of inoculation was tried upon him, the particulars of which will be considered of some interest at the present day.—On the 28th of June 1881, 7 a.m., a night mosquito (*C. pungens*) was found inside the mosquito-net of a fatal case of yellow-fever, in the 5th day of attack. Placed in a glass cage, the *pungens* discharged some black blood upon the sides of the tube, the following day. On the 26th of July, a couple of drops of sterilized distilled water was used to dissolve the dry bloody excrement and the same was soaked up with a small bit of sugar, which looked thereafter as if it had been soaked in black coffee. A freshly caught *C. mosquito* was now introduced in the phial, and went greedily for the sugar. A little more water was now added, turning the sugar into a reddish brown syrup, from which the same *C. mosquito*, in the course of $\frac{1}{2}$ hour had taken a good feed.—On the 29th of July, 2 p.m., L. G. P. one of my 20 non-immunes, was bitten by this *C. mosquito*.—On the 31st of July this man was admitted to the Military Hospital with fever, flushed face, cephalalgia, pain in the back, epigastralgia, injected eyes.—On the 3d of August he had neither fever nor albumin.

than an absolutely incontrovertible demonstration will be required before the generality of my colleagues accept a theory so entirely at variance with the ideas which have until now prevailed about yellow-fever. In the mean time, I beg leave to resume in the following conclusions the most essential points which I have endeavored to demonstrate.

(p. 43)

CONCLUSIONS

1. It has been proved that the *C. mosquito*, as a rule, bites several times in the course of its existence, not only when its bite has been accidentally interrupted, but even when it has been allowed to completely satisfy its appetite; in which case two or more days intervene between its successive bites.

2. Inasmuch as the mouth-parts of the mosquito are very well adapted to retain particles that may be in suspension in the liquids absorbed by that insect, it cannot be denied that there is a possibility that said mosquito should retain upon the setae of its sting some of the virulent particles contained in a diseased blood, and may inoculate them to the persons whom it afterwards chances to bite.

3. The direct experiments undertaken to decide whether the mosquito is able to transmit yellow fever in the above stated manner, have been limited to five attempted inoculations, with a single bite, and they have given the following results: One case of mild yellow-fever, perfectly characterized, with albuminuria and icterus; two cases diagnosed as "abortive yellow fever" by the physicians in charge; and two ephemeral fevers without any definite characters. From which results it must be inferred that the inoculation with a single bite is insufficient to produce the severe forms of yellow fever, and that a final decision as to the efficacy of such inoculations must be deferred until opportunity is found for experimenting under absolutely decisive conditions, outside of the epidemic zone.

4. Should it be finally proven that the mosquito-inoculation not only reproduces the yellow fever, but that it constitutes the regular process through which the disease is propagated, the conditions of existence and of development for that dipterous insect

would account for the anomalies hitherto observed in the propagation of yellow fever, and while we might, on the one hand, have the means of preventing the disease from spreading, non-immunes might at the same time be protected through a mild inoculation.

My only desire is that my observations be recorded, and that the correctness of my ideas be tested through direct experiments. I do not mean by this that I would shun the discussion of my opinions; far from it, I shall be very glad to hear any remarks or objections which my distinguished colleagues may be inclined to express.¹

¹ N. B. The notes do not belong to the original paper.—C. F.



